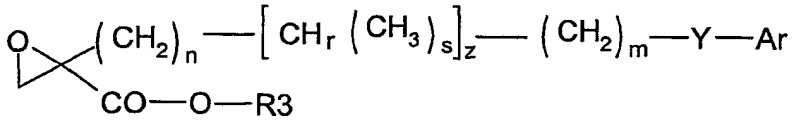
Claims

1. A method of preventing and/or treating a chronic and/or an atopic skin disease by administering an inhibitor of fatty acid oxidation to a patient in a pharmacologically effective amount.

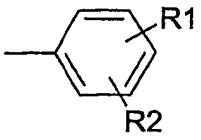
2. The method according to claim 1, wherein the patient is human.

3. The method according to claim 1 or 2, wherein the inhibitor inhibits the expression and/or activity of the enzyme Carnitin-Palmitoyl-Transferase-1 (CPT-1).

4. The method according to claim 3, wherein the inhibitor is an arylalkyl- or aryloxyalkyl-substituted oxirane carboxylic acid of the following formula I



wherein

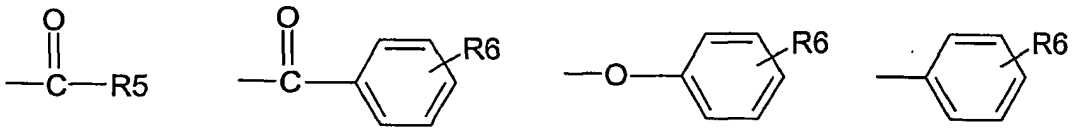
Ar is a substituted phenyl radical 

a 1- or 2-naphthyl radical which is substituted by a radical R4, or

a heterocyclic radical Het;

R1 is a hydrogen atom, a halogen atom, or a 1-4 C lower alkyl group; a 1-4 C lower alkoxy group, a nitro group, or a trifluoromethyl group;

R2 is a hydrogen atom, a halogen atom, or a 1-4 C lower alkyl group; a 1-4 C lower alkoxy group, a nitro group, a trifluoromethyl group, a fully or predominantly fluorine-substituted 1-3 C alkoxy group or one of:



R3 is a hydrogen atom or a 1-4 C lower alkyl group;

R4 is a hydrogen atom, a 1-4 C lower alkyl group, an optionally fully or predominantly fluorine-substituted 1-3 C alkoxy group, or a halogen atom;

R5 is a 1-4 C lower alkyl group;

R6 is a hydrogen atom, a halogen atom, or a 1-4 C lower alkyl group;

Y is the grouping –O- or $-CH_2-$;

z is 0 or 1

s is 1 or 2

r is 2-s

n and m are an integer ≥ 0 with $2 \leq n+m \leq 8$; and

Het is a heterocyclic ring, which preferably has 5 members and is selected from the group consisting of thiophene, thiazole, isothiazole, pyrrole, and, particularly preferably,

pyrazole, and which may carry 1 or 2 identical or different substituents R1;

as well as pharmaceutically acceptable salts and derivatives of said arylalkyl- or aryloxyalkyl-substituted oxirane carboxylic acid.

5. The method according to claim 4, wherein said arylalkyl- or aryloxyalkyl-substituted oxirane carboxylic acid of formula I is 2-(6-(4-chlorophenoxy)hexyl)oxirane-2-carboxylic acid ethyl ester (Etomoxir), 2-(6-(4-difluoromethoxyphenoxy)hexyl) oxirane-2-carboxylic acid ethyl ester, 2-(5-(4-difluoromethoxyphenoxy)pentyl) oxirane-2-carboxylic acid ethyl ester, or 2-(5-(4-acetylphenoxy)pentyloxirane-2-carboxylic acid ethyl ester.

6. The method according to claim 3, wherein the inhibitor is sodium-2(5-(4-chlorophenyl)pentyl-oxirane-2-caboxylate (Clomoxir), Perhexiline, sodium-4-hydroxyphenylglycine (Oxfenicine), or 2-tetradecylglycidate (TDGA), Palmoxirate, Amiodarone and derivatives thereof.

7. The method according to claim 3, wherein said inhibitor is a factor which increases the Malonyl-CoA-levels in the patient.

8. The method according to claim 7, wherein said factor is an activator of the Acetyl-CoA-Carboxylase, an inhibitor of the AMP-Kinase, an inhibitor of the Citrat Synthase, an inhibitor of the Fatty Acid Synthase or an inhibitor of the Malonyl-CoA-Decarboxylase.

9. The method according to claim 1 or 2, wherein said inhibitor inhibits the expression and/or activity of at least one isoform of a fatty acid binding protein (FABP).

10. The method according to claim 9, wherein said at least one isoform of a fatty acid binding protein is psoriasis associated FABP (PA-FABP).

11. The method according to claim 9 or 10, wherein said inhibitor is a substance which binds to FABP.

12. The method according to claim 11, wherein said inhibitor is selected from the group consisting of cis-parinaric acid (cPA), 12-(anthroyloxy)oleic acid (12-AO), or 8-anilino-naphthalene-1-sulfonic acid (ANS).

13. The method according to claim 1 or 2, wherein said inhibitor inhibits the expression and/or activity of Phospholipase A, Lipoproteinlipase, Hormone sensitive Lipase, Monoacylglycerol-Lipase, Acyl-CoA-Synthetase, Canitin-Acylcarnitin-Translocase, Carnitin-Palmitoyl-Transferase-2 (CPT-2), Acyl-CoA-Dehydrogenase, Enoyl-CoA-Hydratase, L-3-Hydroxyacyl-CoA-Dehydrogenase, and/or 3-Ketoacyl-CoA thiolase (3-KAT).

14. The method according to claim 1 or 2, wherein said inhibitor is an antisense oligonucleotide or a dominant negative mutant of at least one of the enzymes CPT-1, Acetyl-CoA-Carboxylase, Phospholipase A, Lipoproteinlipase, Hormone sensitive Lipase, Monoacylglycerol-Lipase, Acyl-CoA-Synthetase, Canitin-Acylcarnitin-Translocase, CPT-2, Acyl-CoA-Dehydrogenase, Enoyl-CoA-Hydratase, L-3-Hydroxyacyl-CoA-Dehydrogenase, or 3-Ketoacyl-CoA thiolase (3-KAT).

15. The method according to claim 1 or 2, wherein said inhibitor is a ribozyme or dsRNA.

16. The method according to one of the preceding claims, wherein the chronic or atopic skin disease is selected from the group comprising psoriasis, cutaneous atopy (e.g. eczema), dermatitis, hand dermatitis, Darrier's disease, Dartroud diathesis, lentigo, xerosis, rosacea, seborrhea, ichthyosis, pigmentation disorders (e.g. hyperpigmentation, melasma, hypopigmentation or vitiligo), actinic keratosis, hyperkeratosis, mycosis fungoides, lichen planus, hyperplasia of the epidermis and other diseases related to inflammatory processes and/or increased proliferation of skin cells.

17. The method according to one of the preceding claims, wherein said inhibitor is administered topically.

18. The method according to one of the preceding claims, wherein said inhibitor is administered in combination with a further therapy.

19. The method according to claim 18, wherein said further therapy is selected form the group comprising the topical treatment with coal tar, dithranol, urea, salicylic acid, and/ or Mahonia aquifolium, the systemic treatment with fumaric acid, fumaric acid esters, and/ or blockers of arachidonic acid, e.g. omega-3 fatty acids and the systemic or topical treatment with steroids, especially cortisone, vitamin D or derivatives thereof, vitamin A or derivatives thereof, vitamin B or derivatives thereof, especially vitamin B12, antibiotics, antimycotics, immunomodulators, e.g. methotrexate, cyclosporine, FK506, E-selectin blockers, P-selectin blockers, ICAM blockers, LFA-1 blockers, LFA-2 blockers, LFA-3 blockers, VCAM blockers,

and/or TNF blockers, with cytokine inhibitors and/or T-cell activation inhibitors.

20. The method according to any one of the preceding claims, wherein the inhibitor is administered together with at least one excipient and/ or auxiliary.

21. The method according to claim 20, wherein the excipient and/or auxiliary is selected from the group consisting of one or more suitable adjuvant(s), one or more pharmaceutically active and/or acceptable carrier(s), diluent(s), filler(s), binder(s), disintegrant(s), lubricant(s), glident(s), coloring agent(s), flavoring agent(s), opaquing agent(s) and plasticizer(s).

22. The method according to any of claims 20 or 21, wherein the inhibitor is administered topically and preferably said at least one excipient and/ or auxiliary is hydrophobic and is preferably selected from the group comprising petroleum jelly, wax, oleyl alcohol, propylene glycol monostearate, propylene glycol monopalmitostearate, isopropyl laureate, isopropyl myristate, isopropyl palmitate, isopropyl stearate, ethyl myristate, propyl myristate, butyl myristate, ethyl oleate, Cetylstearyl alcohol, Vaseline, lanolin alcohol or paraffin oil.

23. Use of at least one inhibitor of fatty acid oxidation for the preparation of a pharmaceutical composition for the prophylaxis and/or treatment of a chronic and/or an atopic skin disease.

24. The use according to claim 23, wherein the pharmaceutical composition is intended to treat a human patient.

25. The use according to claim 23 or 24, wherein said inhibitor is as defined in claims 3 to 14.

26. The use according to one of claims 23 to 24, wherein the chronic or atopic skin disease is as defined in claim 16.

27. The use according to one of claims 23 to 26, wherein said pharmaceutical composition is for topic administration.

28. The use according to one of claims 23 to 27, wherein said pharmaceutical composition further comprises at least one additional active ingredient.

29. The use according to claim 28, wherein said at least one further active ingredient is selected from the group comprising coal tar, steroids, especially cortisone, vitamin D or derivatives thereof, vitamin A or derivatives thereof, vitamin B or derivatives thereof, dithranol, urea, salicylic acid, Mahonia aquifolium, fumaric acid, fumaric acid esters, blockers of arachidonic acid, e.g. omega-3 fatty acids, antibiotics, antimycotics, immunomodulators, e.g. methotrexate, cyclosporine, FK506, E-selectin blockers, P-selectin blockers, ICAM blockers, LFA-1 blockers, LFA-2 blockers, LFA-3 blockers, VCAM blockers, and/or TNF blockers, with cytokine inhibitors and T-cell activation inhibitors.

30. A method for the production of a pharmaceutical composition for the prophylaxis and/or treatment of a chronic or an atopic skin disease, comprising the step of mixing at least one inhibitor of fatty acid oxidation with at least one excipient and/or auxiliary.

31. The method according to claim 30, wherein the inhibitor is as defined in claims 3 to 15

32. The method according to claims 30 or 31, wherein said pharmaceutical composition is for topic administration.

33. The method according to claim 32, wherein said at least one excipient and/ or auxiliary is hydrophobic and is preferably selected from the group comprising petroleum jelly, wax, oleyl alcohol, propylene glycol monostearate, propylene glycol monopalmitostearate, isopropyl laureate, isopropyl myristate, isopropyl palmitate, isopropyl stearate, ethyl myristate, propyl myristate, butyl myristate, ethyl oleate, Cetylstearyl alcohol, Vaseline, lanolin alcohol or paraffin oil.

34. The method according to claims 30 to 33, wherein the method comprises the further step of mixing the at least one inhibitor of fatty acid oxidation and the at least one excipient and/or auxiliary with at least one additional active ingredient.

35. The method according to claim 34, wherein said at least one further active ingredient is as defined in claim 29.

36. A method to investigate the effect of at least one inhibitor of fatty acid oxidation on skin constitution *in vitro*, said method comprising the steps of

a) cultivating cells under conditions essential for cell proliferation
b) adding at least one fatty acid oxidation inhibitor to the cells , and
c) monitoring the proliferation rate of the cells.

37. The method according to claim 36, wherein said cells are keratinocytes or fibroblasts.

38. A method to investigate the effect of an inhibitor of fatty acid oxidation on skin constitution *in vivo*, said method comprising the steps of

a) topically administering at least one fatty acid oxidation inhibitor to the afflicted skin of a skin disease animal model, and

b) monitoring the skin constitution.

39. The method according to claim 38, wherein said skin disease animal model is selcted from the group comprising the SCID mouse engrafted with human psoriatic skin, the BEIGE mouse, the NOA mouse, the NC/Nga mouse, the NC/Nga mouse treated with mite antigens, the fsn/fsn mouse, the IL-18 knock out mouse, the APO-C1 transgene mouse, the APO-C1 knock out mouse, the mouse tail test, the canine atopic dermatitis model, the transgenic mouse line expressing epidermal interleukin-4, the DNFB-induced allergic contact dermatitis in Gottingen minipigs, the hairless rat (WBN/Kob-Ht), the swine inflammation model induced by Phospholipase A2, and the basenji-greyhound (B-G) crossbreed dogs.

40. The method according to claim 38 or 39, wherein the skin condition or formation is monitored by visual inspection, optical coherence tomography (OCT), biopsy, microscopy or ultrasonic or infra-red measuring systems.

41. A pharmaceutical composition for the prophylaxis and/or the treatment of chronic or atopic skin diseases, wherein said pharmaceutical composition comprises at least one inhibitor of fatty acid oxidation.

42. The pharmaceutical composition according to claim 41, wherein the inhibitor is as defined in claims 3 to 15.

43. The pharmaceutical composition according to claim 41 or 42, which further comprises at least one excipient and/or auxiliary.

44. The pharmaceutical composition according to claims 41 to 43, wherein said pharmaceutical composition is intended to act topically.

45. The pharmaceutical composition according to claim 44, wherein said at least one excipient and/ or auxiliary is as defined in claim 33.

46. The pharmaceutical composition according claims 41 to 45, which further comprises at least one additional active ingredient.

47. A pharmaceutical composition according to claim 46, wherein the at least one additional active ingredient is as defined in claim 29.